The human immune system has powerful ability to destroy ‘non-self’ organisms such as cells infected with viruses or bacteria, and abnormal tumor cells. Without precise regulation the immune system can destroy healthy as well as diseased tissue, resulting in autoimmune disease. Regulatory T cells (Treg) are immune cells that help maintain balance in the immune system to prevent destruction of healthy tissue, leading to inflammation and autoimmune disease (Sakaguchi, 2005). While suppression of the immune system is important to prevent the development of autoimmune disease, Treg activity is not helpful during an immune response to infection. Some micro-organisms such as HIV and Tuberculosis bacteria are known to induce down-regulation of Treg cells, so that they can better escape destruction. So a major question in current research is how Treg cells themselves are suppressed or activated.

Treg cells are identified uniquely by expression of the FOXP3 protein, an intracellular transcription regulator. However, Treg cells also express cell surface markers CD4 and CD25, and so they are difficult to separate from CD4+/CD25+ T effector cells. CD127 is used as a marker to distinguish Treg cells from other types of T cells. Early research identified the CTLA-4 protein as responsible for Treg inhibition activity, and in both mice and humans, variants in CTLA-4 are highly associated with autoimmune disease, indicating immune dis-regulation. It is now understood that CTLA-4 on Treg cells suppresses T cell proliferation to diminish an immune response.

Overall, a complex variety of molecular mechanisms contribute to Treg cell-mediated suppression. All these mechanisms can be classified into two major categories:

1. cell-contact-independent mechanisms (production of inhibitory cytokines, blocking IL-2 and ATP/ADP)
2. cell-contact-dependent mechanisms (induction of cytolysis, modulation of antigen presentation cells)

With current interest in using an immune cellular response to better treat disease, research in cell therapy is focused on understanding Treg cells’ recruitment and suppression in targeted tissue. A recent report establishes that CCR5 chemokine recruits Treg cells to a squamous carcinoma cell tumor in mice (de Oliveira et al., 2017), and that mice lacking CCR5 can mount an effective immune response to the carcinoma tumor. This article proposes that suppression of CCR5 in the tumor environment may block recruitment of Treg cells and allow better immune response to the tumor.

Alternatively, recruitment of therapeutic Tregs to a specific target tissue may be used to downregulate an inflammatory immune response, and suppress rejection of a transplanted organ or tissue (Zwang, 2017) or an inflammatory auto-immune reaction such as in Rheumatoid Arthritis. The power to direct Treg cell activity will enable future therapies to enhance or suppress immune response for a variety of diseases.

HemaCare provides high quality isolated regulatory T cells as well as a wide variety of lymphoid cells from peripheral blood that can enhance your research results. For more references to Treg research, see the HemaCare blog: www.hemacare.com/blog/?s=regulatory+t+cells

References:
De Oliveira, CE et al. (2017). Molecular Cancer Therapeutics, September. doi:10, 1158/1535-7163.MCT-17-0341